Controlling human Oesophagostomiasis in Northern Ghana

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-Chapter 1-

General Introduction

Oesophagostomum infections

Oesophagostomiasis is a parasitic disease, caused by infection with nematodes belonging to the genus *Oesophagostomum* within the order Strongyloidae (Durette-Desset *et al*., 1994). Various *Oesophagostomum* spp. have established a parasitic association with a broad range of animals causing nodular worm disease in their large intestines and often result in vast economic loss in animal husbandry (Stewart and Gasbarre, 1989; Orihel, 1970; Goldberg, 1952; Goldberg, 1951; Spindler, 1933; Veglia, 1923).

Differentiation between various *Oesophagostomum* spp. can be made on the basis of adult worm morphological features and molecular characteristics. The head of the adult worm of all *Oesophagostomum spp.* has a characteristic cephalic groove near its proximal gut and a visible "stomum" (secretory pore) at the level of its oesophagus (fig.1.1). This characteristic arrangement of the worm's oesophagus and its "stomum" gives the genus its name viz. "oesophago"- "stomum" (Blotkamp *et al*., 1993; Haupt, 1966; Malik *et al*., 1972; Neuhaus *et al*., 1997).

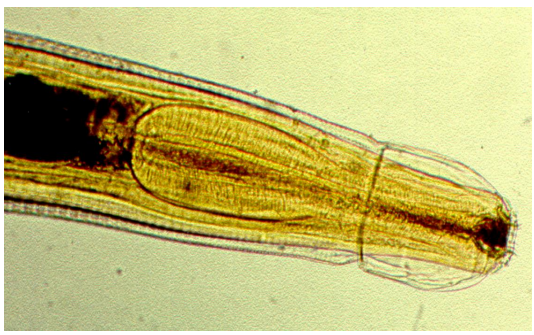

Fig.1.1: The morphological characteristics of an adult worm of *Oesophagostomum bifurcum*. The head of an adult worm showing the cephalic groove with an excretory pore at the level of the oesophagus from which the genus got its name.

The adult *Oesophagostomum* parasites are found in the intestinal lumen of the definitive host as dioecious organisms (Anan-taraman, 1942; Anderson, 1992; Andrews and Maldonado, 1941; Christensen, 1998; Dash, 1973; Dobson, 1966). Eggs are laid and excreted with host's faeces and if deposited onto soil with optimum temperature and humidity, they hatch and moult into infective forms (filariform larvae) within 3-7 days (Barutzki and Gothe, 1998; Fossing *et al*., 1995).

Hosts get infected when the filariform (L_3-larvae) larvae are eaten while grazing in pasture. The ingested L_3-larvae possibly penetrate the gut wall and assume a pathology in animals relating to nodule formation in the intestinal wall has given rise to *Oesophagostomum* infection also being referred to as "nodular worm disease".

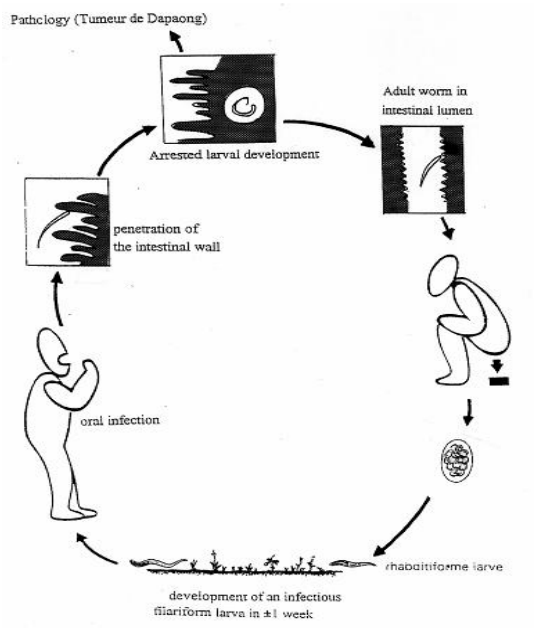

Fig 1.2. The presumable life cycle of *O. bifurcum*

Usually, the entire life-cycle of *Oesophagostomum* spp. is completed in less than 60 days but in few cases, the tissue stage of infection may assume an "arrested phase" of larval development (ALD). ALD would appear to be biological adaptations in the life cycle where eggs are only released when environmental conditions are favourable for transmission to occur thus allowing survival in conditions where environmental extremes would otherwise eliminate infection (Jacobs, 1967; Kendall *et al*., 1977; Michel, 1974; Taylor and Michel, 1953). In some species biphasic histotropic stages have been described in animals, occurring initially in the small intestine and later in the colon (Dash, 1973).

Human oesophagostomiasis

Oesophagostomum infections in humans were discovered in 1902 from autopsy of a 30-year-old east African man. In 1905, the autopsy findings were officially

reported in a publication as the first case of human *Oesophagostomum* infection (Railliet and Henry, 1905). Five years after, another human case was reported in a post mortem of a Brazilian man who died after dysentery (Thomas, 1910). Identification of immature *Oesophagostomum* worms formed the basis for diagnosis but the exact *Oesophagostomum* species responsible for human infection remained uncertain for a while. Adult *Oesophagostomum* worms were first isolated and described in 1911 from stool samples that were supposed to contain adult hookworms recovered from prisoners in northern Nigeria (Johnson, 1913: Leiper, 1911). Several human cases were also reported from around the globe, from Malaysia and Brunei in Asia (Karim and Yang, 1992; Ross *et al*., 1989); from Brazil in South America (Thomas, 1910) and from Zimbabwe, Ethiopia, Ivory Coast and Ghana in Africa (Gordon, 1969; Leoutsakos *et al*., 1977; Baylet and Paillet, 1959; Curan, 1975; Haaf and van Soest, 1964; Barrowclough and Crome, 1979; Gigase *et al*., 1986).

Isolated clinical cases were reported and consequently, human *Oesophagostomum* infection remained to be considered a rare zoonosis, and the adult worms were believed to be unable to develop into adult egg-laying worms in man. A variety of monkey species were implicated as likely sources of human infections (Chitwood, 1970; Habermann and Williams, 1957; Kalter *et al*., 1966).

Several *Oesophagostomum spp.* were named as responsible for causing infections in humans but the precise classifications of these species were not fully established. However, recent taxonomical studies have shown that the commonest species responsible for human oesophagostomiasis in West Africa is *O. bifurcum* whereas *O. aculeatum* and *O. stephanostomum* are the species most commonly responsible for human infections in Asia and East Africa (Lichtenfels, 1980).

Life cycle and pathogenesis

Details of the life-cycle and route of transmission of *Oesophagostomum* infection in humans are lacking, but assumed to be similar to *Oesophagostomum spp.* that infect animals based on comparative experimental infection that humans are infected by ingestion of L_3-larvae through the oral route (Eberhard *et al*., 2001). Ingested larvae pass through two stages of development; a histotropic stage normally occurring in the gut wall and, or, intestinal stage occurring in the

intestinal lumen. The assumed life-cycle of *Oesophagostomum* infection in man is represented in fig. 1.2.

Primarily, type and severity of pathology is related to the tissue stage of infection but the role of lumen dwelling adult worms in causing pathology remains uncertain. The histotropic stage of infection causes nodular lesions due to inflammation. Whether nodule formation is primarily a larval mechanism evolved to evade host tissue immune reactions or it is result of a primary protective function of the host to eliminate the "foreign body" (larvae) remains unclear.

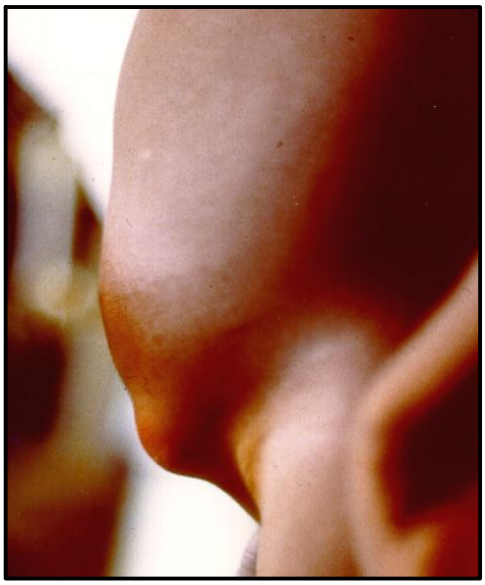

Fig.1.3 An uninodular lesion seen as a Dapaong Tumour in a 7-year old boy.

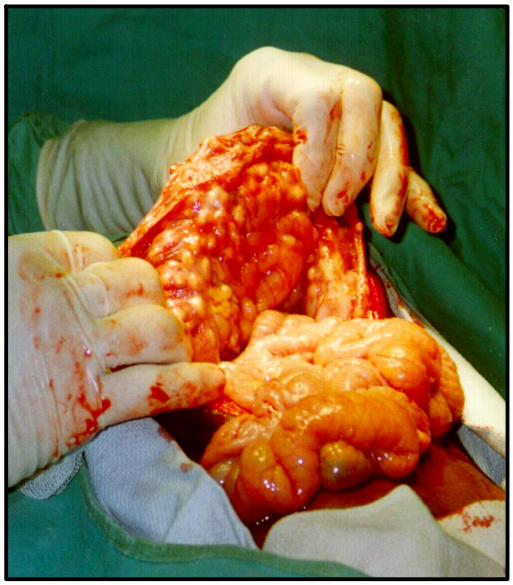

Fig. 1.4.a Multinodular lesions detected in the colon wall following laparatomy.

In the histotropic stage of infection, L_3-larvae commonly invade the colon wall; however tissues of extra-intestinal organs such as the lungs, liver and muscles of the trunk and abdominal walls may occasionally be affected. Palpable and painful protruding masses formed as a result of intense tissue reactions around a nodule containing juvenile *Oesophagostomum* worms is called 'Tumeur de Dapaong'

named after the Togolese northern provincial capital of "Dapaong" where these characteristic lesions were originally described (Gigase *et al*., 1986). Nodular lesions often form adhesions with the abdominal wall and consequently when Dapaong tumour gets supper-infected with gut bacteria, it may even open out as a fistula. When the colon wall get invaded by L_3-larvae, many pea-sized, pus-filled and worm containing nodular lesions within a grossly thickened and oedematous colon may result and is referred to as multi-nodular disease (Haaf and van Soest 1964; Barrowclough and Crome, 1979; Gigase *et al*., 1986). The characteristic Dapaong tumour and multinodular disease are shown in fig. 1.3, 1.4. and 1.4.b. Histological sections of the Dapaong tumour and nodules characteristically reveal juvenile worms at the L_4-L_5 developmental stages. Bowel obstruction, intestinal volvulus (due to formation of multiple nodular lesions in a particular bowel segment) and peritonitis (due to super-infections with gut bacteria) may complicate nodular pathology and present as acute abdominal emergencies.

Fig 1.4b Cross sectional view of a resected part of the colon.
Note the multiple cysts throughout the bowel wall and the intense inflammatory reaction of the surrounding tissue.

Diagnosis of human oesophagostomiasis

Diagnosis of human oesophagostomiasis is difficult and depends on the stage of infection and the associated pathology. Diagnosis of clinical oesophagostomiasis may be made on clinical grounds; however 'typical' clinical symptoms and signs may be mimicked by those of related gastro-intestinal pathologies and vice versa. Commonly, acute oesophagostomiasis presents with fever, weight loss, abdominal pain and persistent diarrhoea and may render diagnosis based on clinical presentations alone inconclusive from other acute abdominal emergencies such as typhoid peritonitis, strangulated hernia, acute appendicitis, perforated peptic ulcer and acute pancreatitis. Exploratory laparatomy was often performed to establish full diagnosis but even after laparatomy, the characteristic nodular lesions in the colon wall may be misdiagnosed for those of abdominal tuberculosis, diffuse colon cancer, amoebiasis and desmoid tumours (Haaf and van Soest 1964; Barrowclough and Crome, 1979; Gigase *et al*., 1986; Storey *et al*., 2000b).

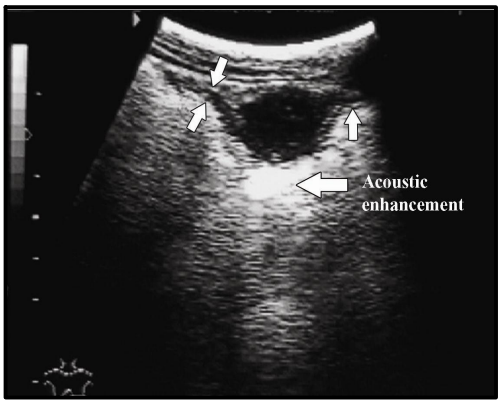

Fig. 1.5 a Sonographic appearance of *O. bifucrum*-induced nodular

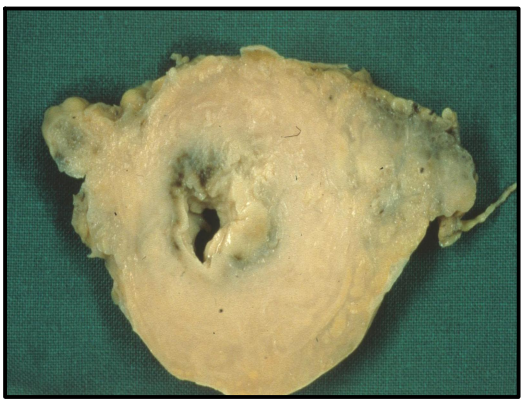

Fig 1.5b Histological appearance of a Dapaong Tumour: a massive fibrotic reaction around an Oesophagostomum nodule (worm not visible)

Abdominal sonographic imaging is increasingly being used to establish diagnosis of human oesophagostomiasis. The choice of this tool is a reflection both of the limitations of the physical examination and improvements in ultrasound technology. Using 5-10-MHz convex array transducers, spatial resolution and image quality are excellent and allow detection of intestinal and abdominal wall nodules (fig. 1.5). Additionally, ultrasound is useful in the evaluation of nodule -type, -size, and -location in the abdomen and in the assessment of the severity of the morbidity (Storey *et al*., 2000b).

Laboratory diagnosis of *Oesophagostomum* infection is hampered by the presence of other parasitic infections in the *Oesophagostomum* endemic areas (especially hookworm).

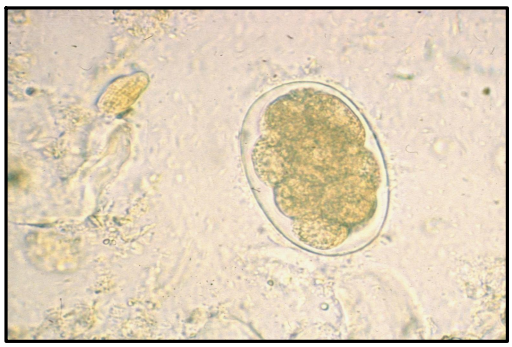

Fig 1.6a. Egg of *O. bifurcum*, not to be differentiated from that of hookworms.

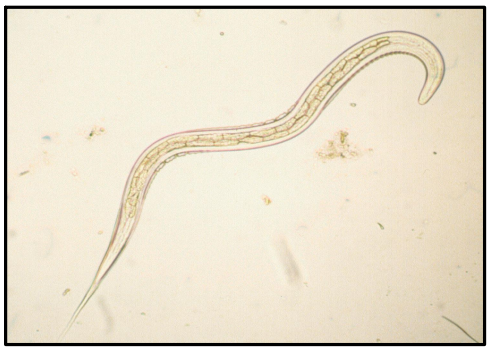

Fig 1.6b. Characteristic L-3 larva of *O. bifurcum*. Note the intestinal cells.

Microscopy can be used to specifically diagnose the presence of adult worms in the intestinal lumen, however direct microscopy of wet stool preparation and Kato smears can not establish definitive diagnosis of *Oesophagostomum* infection because eggs of *Oesophagostomum spp* and hookworm are morphologically indistinguishable. Where both parasites are co-endemic, it is therefore necessary to use coproculture to differentiate the L_3-larvae of both nematodes morphologically using a light microscope under low power magnification based on criteria described by Blotkamp *et al* (1993) (fig. 1.6). Coproculture is prepared by mixing

weighed portions of stool sample with equal volumes of vermiculite or ground charcoal and the mixture incubated at room temperature and under moist condition in a Petridish set-up for 3-7 days (fig. 1.7).

Fig 1.7. Culturing stool samples in the field laboratory in Garu

Serological detection of antibodies against *Oesophagostomum* infection based on the detection of specific IgG_4 and IgE gave promising results but due to several drawbacks these methods were not further developed (Polderman *et al*., 1993; Pit *et al*., 2001). Drawing of blood is not well accepted in the area and besides non-specific reactions were commonly found in non-endemic areas. Molecular method of diagnosis is currently being used but has its own limitations (Romstad *et al*., 1997).

Case Management

Management of human oesophagostomiasis will depend on the stage of the infection, the associated signs and symptoms and expected complications. For the treatment of uncomplicated oesophagostomiasis, 400 mg of albendazole, a benzimidazole anthelminthic that is relatively well absorbed and metabolised to other active anthelminthics (e.g. albendazole sulphoxide), is the drug of choice. In complicated oesophagostomiasis, dosage depends on the severity of disease; in acute oesophagostomiasis without acute abdomen, 200-400mg of albendazole given immediately and continued for up to 5 days in combination with amoxicillin (250mg for 5days) has been used (Storey *et al*. 2000a). When oesophagostomiasis presents as acute abdomen, laparatomy, followed by bowel resection and anastomosis is the preferred management (Haaf and van Soest 1964; Gigase *et al*., 1986). Complicated Dapaong tumours may result in the formation of periumblical

abscesses or fistulae. Incision and drainage through the skin accompanied by rigorous albendazole and antibiotics treatment is used.

Human oesophagostomiasis in Ghana and Togo

The first case of human oesophagostomiasis in the region was reported from Bawku Hospital in the Upper East Region in 1964 (Haaf and van Soest 1964). By the late 1980s, several other cases had been reported from Bawku hospital in Ghana and from the provincial hospital in Dapaong (about 40km from Bawku) in the neighbouring Republic of Togo. These cases were diagnosed clinically by recognising the impressive and classical painful mass in the lower abdomen; subsequently juvenile worms recovered from the nodules were recognised as *Oesophagostomum spp* (Haaf and van Soest 1964; Barrowclough and Crome, 1979; Gigase *et al*., 1986).

Initially, humans were thought to be accidental hosts with monkeys acting as the definitive hosts (Chitwood, 1970; Habermann and Williams, 1957; Baylet *et al*., 1959; Kalter *et al*., 1966). Attempts to understand the epidemiology, biology of transmission and clinical presentation and management of the disease showed that oesophagostomiasis was an endemic disease of humans in this part of the world (Polderman *et al*., 1991; Krepel *et al*., 1992; Pit *et al*., 1999a). The symptoms and signs of the disease were familiar to the indigenous population and native healers even attempted to cure the disease. They referred to the disease in various local dialects implying that they were familiar with the disease and that it was fairly common in the area (Polderman *et al*., 1991).

An area-wide survey showed that an estimated 25% of the population living in North eastern Ghana and North western Togo was infected and a million more at risk. In many villages, *O. bifurcum*-prevalence was as high as 70%. Abdominal ultrasound investigations to measure the pathology due to *O. bifurcum*, demonstrated that pathological lesions can be visualized in up to 40% of the infected populations. In most *O. bifurcum*-endemic villages, hookworm -prevalence and -intensity is also extremely high with more than 80% of the population infected (Polderman *et al*., 1991; Polderman *et al*., 1999; Pit *et al*., 1999a; Storey *et al*., 2001c; Yelifari *et al*., 2005). In Nalerigu hospital in the endemic area, 0.2% of cases reporting at the out patient department are due to

human oesophagostomiasis and 1% of these require surgical intervention (Storey *et al*., 2000a).

Many aspects of the transmission biology of *O. bifurcum* in man require further research. It is not known why the distribution of *Oesophagostomum* infection remains localized within the present endemic area and why it is found nowhere else in the world. Are behavioural factors responsible, are there specific soil conditions in this area which favour the larval development and which are lacking elsewhere?

Controlling human oesophagostomiasis and hookworm infections

In recent times, infection with soil transmitted helminths has been increasingly recognised as an important public health problem. The most important helminthiasis in developing countries are due to infection with geo-helminths viz. hookworms (both *Necator americanus* and *Ancylostoma duodenale*), roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichuria*) and to schistosomiasis mainly due to *Schistosoma mansoni* and *S. haematobium* (M.S. Chan *et al*., 1994; de Silva *et al*., 2003). It has been estimated that more than 2.0 billion people worldwide are infected with at least one of these helminths, with hookworm alone infecting more than 1.3 billion people (WHO, 1996; Bundy, 1996). The morbidity of infection found to be related to the infection-type and worm load as well as the physiological requirement of infected individuals (Hotez *et al*., 2003). In hookworm infection for instance, menstruating women, young children and infants are particularly susceptible because of the high nutritional requirements for both physical and mental development, pregnancies, lactation and compensation of cyclical menstrual blood loss (Stephenson *et al*., 2000).

In northern Ghana and Togo, the situation is compounded by the fact that *O. bifurcum* and *N. americanus* are co-endemic in humans and cause significant morbidity (Polderman, 1993; Krepel 1992; Yelifari *et al*, 2005). More than quarter of a million persons in this endemic area are infected with *O. bifurcum* and village prevalence of hookworm could be as high as 90% (Pit *et al*., 1999a).

Over the past years, experience and lessons learned from global helminth control programmes such as those in Zanzibar islands, Seychelles archipelago and Sri Lanka have been extrapolated in several countries (Albonico *et al*., 1994; Albonico *et al*., 1996; Stoltzfus *et al*., 1997). Currently knowledge of the control of

human oesophagostomiasis is lacking altogether. This is partly due to the fact that distribution of *O. bifurcum* infection is limited to a small region of northern Ghana and Togo and partly to the limited knowledge about the life-cycle of the worm.

Following a regional conference organised in Ghana in 1998, the health authorities in Ghana and Togo wished to control human oesophagostomiasis which posed significant public health problems in their area (Polderman *et al*., 1999). Before embarking on area-wide control activities, a study was required to explore the potential of controlling human oesophagostomiasis through repeated albendazole mass treatment. Such study is the subject of this thesis.

The study area and people

The study was conducted in the Worrikambo sub-district of the present Garu district of the Upper East Region of Ghana. Garu had been part of the Bawku East Municipality with Bawku as the municipal capital but towards the end of 2004, the Garu/Tempani district was created by splitting the Bawku municipality into two districts with Garu as the new district capital. Our study covered 29 villages situated about 15km south of the Garu Township located between latitudes N10.837° and N10.689° and longitudes W0.081° and W0.226°. The borders of the area are delineated by the Gambaga scarp to the south, and the Ghana-Togo border to the east. To the north and to the west, the borders of the study area were determined to limit the total population to some 20, 000 persons. A map of Ghana showing the study area and the distribution of compounds over the area is shown by fig.1.8 and a pictorial of a typical Bimoba village and compound is shown in fig.1.9.

The area is a lowland area, 210-270m above sea level, just north of the Gambaga Escarpment. The vegetation consists of tall grasses with scattered fire resistant trees such as the shea tree, the "majestic" baobab tree and the dawadawa predominating amongst a heterogeneous collection of other trees which provide most domestic requirements of fuel wood, charcoal, and wood for the construction of houses, cattle kraals etc.

The climate is typically sub-sahalian characterized by dry and rainy seasons annually. Around December, cold dry winds, the Harmattan, blow from the Sahara Desert and temperatures can drop to about 12ºC in the early morning. The

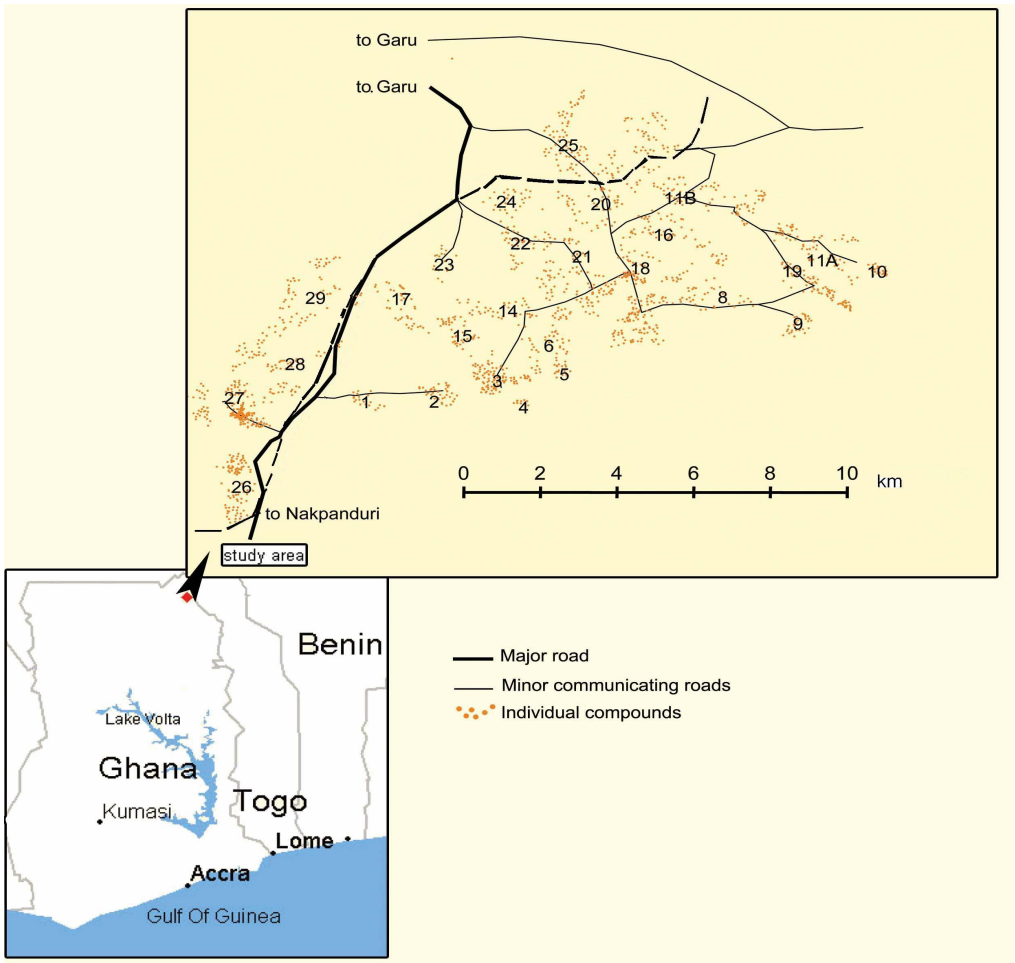

Fig. 1.8 Map of Ghana showing the intervention and the control areas
The numbers in the map represent village numbers; the broken line represents the boundary between the intervention area (villages 1-24) and the control area (villages 25-29)

Harmattan, with its very low humidity, dries up all the vegetation in the district and the relative humidity may drop to values as low as 20%, predisposing the district to large-scale bush fires that now occur annually (Ghana Statistical Service, CWIQ, 1998). In the hottest months of March-April, the daily temperature may reach 42ºC in the shade.

Rains begin in mid-May and end in late October with an annual rainfall range of 800mm to 1000mm and a relative humidity of about 80%. No rainfall occurs for the remainder of the year so the period just before the next rainy season is always a period of very low food availability.

The 2002 Ghana Population and Housing Census puts the population of the Garu district to about 60,162 representing an inter-censal growth rate of 1.26% between 1984 and 2000. Illiteracy is high and approximately over 95% of adult females in the area have never attended school - the national average is 52.6%. Over 70% of the population is subsistence farmers. Land fertility is very poor and the rainfall period is very short causing a seasonal migration of the youth to other regions and a high seasonal child malnutrition rate of between 37% - 57% (Ghana Statistical Service, CWIQ, 1997).

In the health sector, staff per facility amount to only one third to half of the national average indicating a serious lack of health care personnel of all categories due to unattractiveness of the area in terms of resources or incentives. Maternal mortality, infant mortality and child mortality rates are among the highest in the country between 5-10/1000, 103 and 132 respectively (Ghana Statistical Service, CWIQ, 1998). Some health provision in this area is provided by Government but most comes from the mission health care system dominated by the Presbyterian Mission of Ghana. The only hospital in the area, the Bawku Hospital, in addition to other health centres in Garu, Widana and Wuriyanga, Bugri, Pusiga and Binduri are ran by the Presbyterian Church.

Given the district proximity to two neighbouring countries, economic activities are high and HIV/AIDS is a matter of concern. Though the prevalence rate is about 3.1%, below the national average, there is still cause for alarm because there has been no significant change in local life styles and some negative traditional practices such as female genital mutilation and polygamous marriage.

Subjects and methods

Because data on civil registers are not readily available for the area, a project-based demographic surveillance study was conducted in April 2001. All villages and compounds in the area were mapped with GPS (Global Positioning System) and unique identification numbers were assigned to identify them. Following the demographic registration, a cross sectional survey involving ~10% of the registered population was conducted in September 2001. All selected persons underwent parasitological and clinical examinations to obtain baseline infection and morbidity data before embarking on mass treatment. Subsequently, the study area of 29 villages was split into an intervention area comprising 24 villages and a control area comprising 5 villages. Fig.1.8 shows a map of the study area showing the intervention and the control areas. Fig. 1.9 gives an impression of a characteristic Bimoba village.

The demographic registration

All villages in the research area were given village identification numbers (VID). Within a village, our field team made compound visits with the help of village volunteers. All compounds were identified by unique compound identification numbers (CID) and GPS used to register their coordinates in terms of longitudes and latitudes. Inhabitants of the registered compounds were also registered and identified by individual identification numbers (ID). The individual numbers were serially generated from the compound and village numbers such that an individual from the village with VID = 18 who lives in the forty-fifth compound (0045) was given an Id number of 18045001.

This numbering system was designed by the project in collaboration with the area local traditional (chiefs) administration. In addition, basic demographic information concerning the number of persons living and present in the compound, age and gender, tribal background, occupation, duration of stay in the village and the use of health facilities in the area were recorded using semi-structured questionnaire forms.

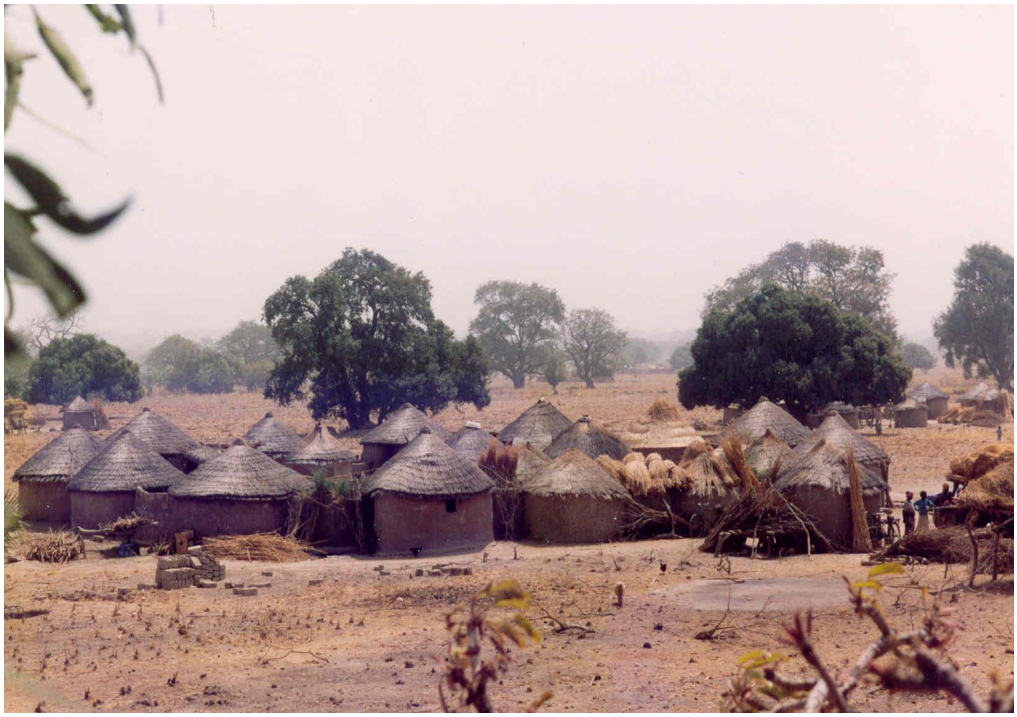

Fig.1.9 A characteristic Bimoba compound in one of the villages of the study area.

The parasitological and clinical surveys

Parasitological and clinical surveys were carried out in September and October each year for two reasons: first, this period coincides with the end of the rains when worm loads are known to be highest. Secondly, maintaining a specific time of the year is vital to offset the effects of seasonal variation of *O. bifurcum* infection described earlier (Pit *et al*., 1999b; Pit *et al*., 2000c).

After all compounds and subjects were registered in the area, 10% of them were randomly selected through a cluster sampling procedure with the compound as the sampling unit. The inhabitants of selected compounds were summed up and when the sum of all inhabitants of the sampled compounds in a particular village fell short of the expected 10% of the registered village population, additional

compounds were added. In the selected compounds, all inhabitants were included in the study.

Sampled compounds were visited by project field workers and each inhabitant was given a labelled plastic container to produce a stool sample for laboratory examination. From each stool sample, a single 25-mg Kato smear was prepared and examined for the presence and number of helminths eggs. Eggs of hookworm and *O. bifurcum* are morphologically identical, differential diagnosis had to be based on coproculture. On the day the stool samples were received, 6-gram sub-samples were mixed with equal volumes of Vermiculite; the mixture was divided into three equal portions (2 gram each) and cultured in three Petri dishes. Two of the cultures were examined 5–7 days later, at low power (x100) by two different microscopists. The third culture was a back up in case a culture was spoiled due to gross contamination with maggots or fungi. The third-stage larvae of *O. bifurcum*, hookworm and *Strongyloides stercoralis* were identified, differentiated and the number of *O. bifurcum* and hookworm larvae was counted according to the procedure used by Blotkamp and co-workers (1993).

All individuals who underwent stool examination were also invited to attend a mobile field clinic to be examined by ultrasound. A Kretz technology LS portable ultrasound machine (Kretztechnik AG, Austria) equipped with a 3-5 MHz convex transducer and powered by a generator was used to scan the abdomen with the patient in the supine position for the presence of *O. bifurcum* -induced nodular pathology. A standardized imaging protocol was used during ultrasound investigations. Bimanual abdominal palpation preceded all ultrasound investigations

Mass treatments

In late October 2001, in April 2002 and in November 2002 all inhabitants in the intervention area were offered treatment with a single 400 mg oral dose of albendazole (Zentel®, GlaxoSmithKline, Mayenne, France). In the control area, no mass treatment took place but individuals examined and found to be infected with *O. bifurcum* and/or hookworm were also offered treatment. In April 2003, as part of the global campaign to eliminate lymphatic filariasis, mass treatment was given by the Lymphatic Filariasis Elimination Programme to all inhabitants living in the

O. bifurcum-endemic area in northern Ghana and northern Togo (including both the intervention and control areas). This round of treatment consisted of 400 mg albendazole and 10 mg ivermectin. This treatment seriously interfered with the original design of the study and as a consequence the final objectives of the study had to be redefined (see next paragraph).

Monitoring of effects of treatment

The impact of treatment was measured at two different levels: infection was measured with the use of coproculture identifying the presence of characteristic L3-*Oesophagostomum*-larvae and morbidity with the use of ultrasound to monitor the presence of the characteristic nodular lesions.

In September 2002, after two rounds of albendazole mass treatment had been completed and in September 2003, after two further rounds of treatment had been completed, 5% cross sectional surveys were conducted to measure the impact of albendazole mass treatment on *O. bifurcum*- and hookworm- infections. In September 2004, a last survey was conducted to measure the re-infection rate for *O. bifurcum* and hookworm 18 months after the last treatment. The subjects examined in September 2003 were re-examined in September 2004. In September 2002 and 2004, individuals who were examined by coproculture were also invited to undergo abdominal ultrasound examination to determine the impact of treatment on *O. bifurcum*- induced nodular pathology. In September 2003, due to time and logistics constraints, only stool examinations were carried out.

The impact of treatment was monitored by measuring the percentage change in prevalences and intensities of *O. bifurcum* infection and, by way of comparison, of that of hookworm, and by monitoring the changes in the rates of ultrasound-visible pathology. Each time, at follow-up, prevalences and intensities of infection in the intervention area was compared with baseline levels and those measured in the control area, where no mass treatment had taken place before April 2003. The programme outline and design of the project is given in fig. 1.10.

The thesis

Following the discovery of human oesophagostomiasis as a common human nematode in northern Ghana and northern Togo, several papers have been published concerning the epidemiology, clinical presentations, diagnosis and management of the disease in the area (Haaf and van Soest, 1964; Gigase *et al*., 1986; Polderman *et al*., 1991; Krepel *et al*., 1992; Pit *et al*., 1999a,b; Storey *et al*., 2000a; Verweij *et al*., 2000; Verweij *et al*., 2001; de Gruijter *et al*., 2004; Yelfari *et al*., 2005). Attempts to develop strategies to control the disease in this area were made but until now, our knowledge on infection- and morbidity- control remains scanty.

There are several reasons why control of human oesophagostomiasis in this area is an important challenge. First of all, the prevalence of *O. bifurcum* infection is pretty high, even among the very young children implying that transmission of infection is intense in this area. Secondly, in contrast to other rare human nematode infections such as *Ternidens* and *Trichostrongylus*, the clinical implications of human *Oesophagostomum* infection are significant. Thirdly, control of oesophagostomiasis would seem more rewarding as the parasite appeared to be relatively fragile compared to hookworm and other related soil transmitted nematodes.

Before embarking on albendazole-based mass treatment, the epidemiology of *O. bifurcum* and hookworm infections in this area that were only briefly considered in earlier studies are further investigated and analysed in more detail. One reason for detailed analysis is to explore ways of prevention, requiring a better insight in the route of transmission *of O. bifurcum*. The association with hookworm infection appeared to be the rule in several studies and suggests a similarity in routes of transmission, i.e. percutaneous rather than oral. Another even more important reason to carry out a careful epidemiological study was to create a baseline for monitoring the impact of intervention.

The use of ultrasound to detect *O. bifurcum*-induced nodular pathology greatly improved diagnosis and management of clinical cases of human oesophagostomiasis. Clearly, ultrasound is a useful epidemiological tool to measure and monitor morbidity due to *O. bifurcum* infection at the population level but earlier sonographic studies failed to establish a correlation between egg count

fig.1.10 **next page.**

Summary of surveys and mass treatment schedules used to evaluate the anthelminthic treatment of the intervention population and the controls (next page!).
This figure gives an overview of the final design of the treatment monitoring studies and the times of treatments and surveys.

Pink:	Baseline surveillance
Blue:	parasitological surveys
Green:	Ultrasonographical surveys
Pale yellow:	OIRP-based mass treatment with albendazole
Dark yellow:	LF-based mass treatment with albendazole-ivermectin.

N.B.
On top of the main stream of programme activities, summarized in this figure, a small scale study was done to evaluate the efficacy of albendazole treatment for *O. bifurcum* and hookworms in a time frame short enough to exclude the confounding role of re-infection. This study was performed just north of the study area of the villages 1-29. The results are presented in chapter 5.

The original study design aimed at demonstration of different rates of re-infection with *Oesophagostomum* and hookworm in the intervention area and at demonstration of reduction of transmission in the mass treatment area in comparison with re-infection in subjects treated in the control villages, where transmission remained uninterrupted.

Due to the unforeseen interference with albendazole-ivermectin treatments of the Lymphatic Filariasis Elimination Programme, the last part of the original programme was modified into operational research on a programme to control human oesophagostomiasis in northern Ghana as a whole.

date	Intervention group villages 1-24	Control group villages 25-29	
April 2001	Census registration (13612 subjects)	Census registration (3000 subjects)	
September 2001	Baseline Parasitological Survey: 1011 examined	Baseline Parasitological Survey: 303 examined	Ultrasound exams
October 2001	First Mass Treatment 10671 treated (78.8%)	No Mass Treatment	
April 2002	Second Mass Treatment 11144 treated (76.3%)	No Mass Treatment	
September 2002	First Parasitol follow-up 535 persons examined	First Parasitol. Follow up 173 persons examined	Ultrasound exams
October 2002	Third Mass Treatment 11064 treated (70.8%)	No Mass Treatment	
October 2003	LFEP-based Mass Treatment: approx. 72%	LFEP-based Mass Treatment: approx. 72%	
September 2003	2nd Parasitol. follow up 478 persons examined	No Parasitological follow up	
September 2004	Last Parasitol. Follow up	Last Parasitol. follow up	Ultrasound exams
October 2004	Area-wide surveillance in Sentinel villages in Northern Ghana, beyond the main area of research		
November 2004	Treatment by the LFEP End of actual Oesophagostomum Research		

Figure 1.10

and severity of pathology. Concurrent coproculture analysis will help to assess a possible correlation between egg and larval count and severity of nodular pathology at the individual level.

Effective control of *O. bifurcum*-infection and -morbidity through mass treatment requires that the drug should be easily available, cheap, and easy to apply. It should have a high efficacy and the parasite should not readily develop resistance to treatment.

Few data are available on cure rates of single dose regimens of albendazole for *O. bifurcum* infections. Before embarking on full scale control, a comparative evaluation of the impact of treatment on *O. bifurcum* and hookworm infections three weeks after treatment was necessary to establish baseline information for future comparison.

Ultimately, the goal for mass treatment with albendazole is to achieve reduction in the prevalence and intensity of *O. bifurcum* and hookworm infections and related morbidity markers. Albendazole has been shown to be effective in the treatment of clinical oesophagostomiasis by killing adults and presumably the tissue stage larva. In hookworm, large-scale treatment was shown to be effective but frustrated by rapid re-infection due existing reservoir of infection. Since the reservoir of infection is comparatively smaller for *O. bifurcum* than for hookworm in the area, it was anticipated that repeated mass treatment could possibly break the transmission cycle of *O. bifurcum* leading to infection control. For hookworm, transmission may not be broken but could be kept at low level to reduce morbidity.

Factors such as the focal distribution of *O. bifurcum* infection and the fragility of its life cycle may favour control of *O. bifurcum* transmission and morbidity but not hookworm. We anticipate that repeated albendazole mass treatment would lead to an initial drop of prevalence and intensity of infection in the short-term but once treatment is stopped re-infection is bound to take place. The analysis of the rate of re-infection with *O. bifurcum* in comparison with that of hookworm is core of the present study.